REMARKS

The present application relates to prevention of pathangiogenic conditions by administering group B β-hemolytic *Streptococci* toxin receptors or immunogenic fragments thereof, to compositions comprising such fragments, as well as to methods of producing the compositions. Claims 1, 4-16, 29-38, and 40-56 are pending. Claims 49-54 are withdrawn from consideration. Based on the following remarks, applicant respectfully requests reconsideration and allowance of the claims under prosecution.

Claim Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejects Claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner maintains that the mouse *in vivo* experimental data provided in the specification and showing tumor suppression in mice is not enabling for the claimed compositions and methods. The Examiner asserts that the specification is not enabling because mouse models cannot be used to reliably predict the outcome of human treatments. Applicant respectfully disagrees.

It is the applicant's position, supported by the current case law, that human testing is not required to obtain a patent. See *Scott v. Finney*, 34 F.3d 1058, 1063. The outcome of human treatments, including safety and efficacy, is assessed in clinical trials that are regulated by the corresponding government agencies. For the purpose of assessing the enablement aspect of patentability, an animal model should be accepted as correlating to a specific conditions, unless the Examiner has evidence that one skilled the art would not accept the model as reasonably correlating (MPEP 2164.02).

The Examiner cites a 1997 article by Gura ("Systems for Identifying New Drugs Are Often Faulty" *Science*, v. 278, 1041-1042 (1997); hereinafter *Gura*) as evidence that animal xenograft cancer models do not correlate with human cancer for the purpose of screening candidate therapeutic agents. Applicants respectfully bring to the Examiner's attention that *Gura* deals primarily with screening of large numbers of cell-killing compounds in order to

identify anti-cancer drugs. In contrast, the present application deals with the field of anti-cancer vaccines, more particularly, with immunogenic peptides that are used to induce or maintain an immune system to protect from, prevent, or attenuate a pathangiogenic condition, such as cancer. As *Gura* does not deal with the field of anti-cancer vaccines, it fails to support the lack of correlation asserted by the Examiner for at least this reason. Additionally, later studies superseded *Gura* by providing improved mouse models. See, for example, Wilkinson *et al.*, "Antibody Targeting Studies in a Transgenic Murine Model of Spontaneous Colorectal Tumors" *Proc. Natl. Acad. Sci. U. S. A.* v. 98, 10256-10260 (2001), specifically stating that its model overcame the limitations discussed in *Gura*

In the field of anti-cancer vaccines, mouse models are widely used and are considered reasonably predictive of the vaccines' future therapeutic utility. See, for example, Niethammer *et al.*, "A DNA Vaccine Against VEGF Receptor 2 Prevents Effective Angiogenesis and Inhibits Tumor Growth" *Nature,* v. 8, 1369-1375 (2002) (hereinafter *Niethammer*), stating that the mouse testing data shows that VEGF receptor is a suitable target for anti-cancer immunotherapy. See also the reviews by Finn and Forni ("Prophylactic Cancer Vaccines" *Current Opinion in Immunology*, v. 14, 172-177 (2002); hereinafter *Finn*) and by Dranoff ("Immune Recognition and Tumor Protection" *Current Opinion in Immunology*, v. 14, 161-162 (2002); hereinafter *Dranoff*), both citing multiple mouse model studies around the time of filing of the present application. Thus, in the field of anti-cancer vaccines, mouse models are considered by those skilled in the art as reasonably correlating with the human pathangiogenic conditions, such as cancer.

The Examiner distinguishes the present case from *in re Brana*, 51 F.3d, stating that, in contrast to *in re Brana*, there does not appear to be reasonable presumption of the utility of the claimed invention. Applicants respectfully disagree. Data from *in vitro* or animal testing is generally sufficient to support therapeutic utility. If one skilled in the art would accept the animal tests as being reasonably predictive of utility in humans, evidence from those tests should be considered sufficient (MPEP 2107.03). *Finn, Forni*, and *Dranoff* all maintain (see the respective abstracts) that animal model data indicates the usefulness of cancer vaccines

for the anti-cancer therapies. *Fynn* specifically mentions that cancer vaccines were most effective in protection from tumor challenge in animal models, and that this observation was recapitulated in human trials. *Finn* concludes that cancer prevention is the most promising avenue for the use of cancer vaccines. Thus, those of skill in the art consider animal testing data as reasonably predictive of utility in humans in the field of anti-cancer vaccines. Therefore, the mouse studies provided in the specification should be considered sufficient to support the utility in humans. Based on the provided animal model data, one of skill in the art would recognize that there is a reasonable presumption of utility of the applicant's claimed invention.

The Examiner further asserts, distinguishing from *in re Brana*, that a skilled artisan would be required to perform more than conventional experimentation to determine optimally safe and effective dosages and schedules for administration [of the applicant's immunogenic compositions to human subjects]. But establishing the safe and effective dosages and schedules is a matter of clinical testing. Clinical testing is a well-established field controlled by the corresponding government agencies. MPEP 2107.03 provides that, for the purpose of establishing utility, "[o]ffice personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials." Moreover, human therapeutic vaccine trial parameters are known to those skilled in the art (see *Dranoff*, citing Jäger *et al. Current Opinion in Immunology*, v. 14, 178-182 (2002)), parameters for the human clinical trials were developed as early as in 2000 (see, for example, Jäger *et al.*, "Monitoring of CD8 T Cell Responses to NY-ESO-1: Correlation of Humoral and Cellular Immune Responses" *Proc. Natl. Acad. Sci. U.S.A.*, v. 97, 4760-4765 (2000)). Thus, one of skill in the art would know that establishing clinical testing protocols of the applicant's claimed anti-cancer vaccines is conventional and not undue experimentation. One of skill in the art would also know also that clinical testing is not necessary for a reasonable presumption of utility of the applicant's claimed invention.

The Examiner states that the publication by Fu *et al.* "Identification of a Novel Membrane Protein, HP59, with Therapeutic Potential as a Target of Tumor Angiogenesis"

Clinical Cancer Research, v. 7, 4182-4194, (2001) (hereinafter *Fu*) shows that the applicant's claimed invention cannot be used to prevent cancer in mice. The Examiner specifically refers to Figure 6. Figure 6 shows attenuation of tumor growth upon immunization of mice with the applicant's claimed immunogenic peptides. *Fu* also states on pages 4189-4190 that histological examination showed no sign of toxicity or abnormality in the immunized mice except for those expected from the immunization. In the immunized mice, pathangiogenesis and concomitant vasculogenesis were effectively inhibited, and the tumors used existing normal vessels for its nutritional needs. The Examiner asserts that *Fu* shows that the applicant's immunogenic peptides were only effective in attenuating tumors, not in preventing cancer. Applicant respectfully disagrees.

In general, cancer is a complex pathological phenomenon characterized, among other manifestations, by uncontrolled tumor growth and dissemination of metastases. This process is supported by neovascularization, or angiogenesis. As restated in *Niethammer*, angiogenesis is a rate-limiting step in the development of tumors. In the absence of angiogenesis, tumor growth is generally limited to 1-2 mm^3, with tumors often becoming necrotic and apoptotic after reaching this size. In the absence of angiogenesis, tumors fail to establish metastases, which need blood supply for growth. Small, self-contained tumors are unlikely to metastasize, generally present little danger to a patient, and, in many cases, are not detected. Thus, the present invention provides methods and compositions for cancer prevention and attenuation by providing treatments that preventively contain tumor growth and keep in check angiogenesis, averting the establishment of metastases and the adverse physiological effects of tumor growth. This is evidenced in *Fu*, for example, by lack of cancer pathology in the immunized mice. More specifically, the claimed method and composition prevent the pathologic condition of cancer by causing an immune response that attacks abnormal blood vessels such as those that provide nutrients to a growing tumor. Thus, contrary to the Examiner's assertion, *Fu* supplies ample evidence that the applicant's immunogenic compositions are effective in preventing angiogenesis and pathology characteristic of cancer. In general, shown in *Fu* inhibition of tumor growth and reduction in

dissemination and growth of metastases are the criteria accepted in the field of cancer vaccines for characterization of effective protection from cancer (see, for example, *Niethammer*). *Fu* supports the applicant's enabling disclosure, not contradicts it.

In view of the foregoing, applicant respectfully asserts that the disclosure of the present application is enabling and contains working examples commensurate in scope with the claims. The specification provides sufficient guidance to a skilled artisan to make and use the claimed invention without undue amount of experimentation. Applicant respectfully requests that the rejection of Claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. § 112, first paragraph, be withdrawn.

CONCLUSION

Applicant is of the opinion that the Office Action has been completely responded to and that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned at (404) 815-6102 is respectfully solicited.

Respectfully submitted,

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